

Claims

1. A linear concatamer of at least two non-identical DNA sequences which, by virtue of third base redundancy of the genetic code of the codons, each encode the same polypeptide of at least 30 amino acids; wherein the concatamer comprises or consists of a nucleic acid sequence which codes for an oligomer of said polypeptides in a continuous reading frame.
2. A concatamer according to claim 1 to which a single invariant cysteine codon has been added to one DNA sequence to encode a polypeptide derivative with a unique unpaired cysteine.
3. A concatamer according to claim 2 in which the added cysteine codon is located at the 3' end of the sequence to encode a cysteine at the C-terminus of the corresponding polypeptide.
4. A concatamer according to any of claims 1 to 3 in which the concatamer is fused to one or more sequences encoding one or more antigens.
5. A concatamer according to claim 1 in which the concatamer is fused to one or more sequences encoding one or more antigens and a single cysteine codon has been added to or inserted in-frame in only one antigen coding sequence.
6. A concatamer according to claim 4 or 5 fused to one sequence coding one antigen.
7. A concatamer according to any of claims 1 to 6 in which the DNA sequences in the concatamer encode the complement C3 fragment C3d or an analogue thereof.

8. An expression vector comprising a concatamer nucleic acid sequence according to any of claims 1 to 7 and regulatory or other sequences for expression of any oligomeric polypeptide encoded thereby.
- 5 9. A host cell comprising an expression vector according to claim 8.
10. A method of making a concatamerised polypeptide, the method comprising expressing a concatamer according to any of claims 1 to 7 from a host cell according to claim 9, and isolating the expressed product.
- 10 11. A method of making a concatamerised polypeptide, the method comprising expressing a concatamer according to claims 2 to 6, isolating an expressed polypeptide having a unique unpaired cysteine and at least one antigen, homo- or hetero- dimerising the isolated polypeptide through formation of an intermolecular disulphide bond, and isolating the dimerised polypeptide.
- 15 12. A method of making a concatamerised polypeptide, the method comprising expressing a concatamer according to claims 2 to 6, isolating an expressed polypeptide having a unique unpaired cysteine and at least one antigen, conjugating the unique cysteine residue in the isolated polypeptide to a chemical linker group comprising at least two thiol-reactive functions, and isolating the conjugated polypeptide.
- 20 25 13. A method of making a chemically reactive concatamerised polypeptide, the method comprising forming a DNA construct, the construct being formed by fusing a concatamer according to claim 1 in-frame firstly to a DNA sequence encoding a self-splicing
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intein polypeptide and secondly to a DNA sequence encoding a protein domain with a ligand specificity useful for affinity chromatography, expressing the DNA construct, and isolating the expressed fusion polypeptide by chromatography on an immobilised ligand which has specificity for said protein domain.

14. A method for making a chemically reactive adjuvant concatamerised polypeptide according to the method of claim 13, wherein the concatamer encodes repeated polypeptide units which are C3d or another ligand of CR2 (CD21), and wherein the concatamer is fused to a bacterial intein sequence and fused to a chitin binding domain, and wherein the expressed fusion polypeptide is isolated by affinity chromatography on immobilised chitin.
15. A method of making a concatamerised polypeptide, the method comprising coupling the isolated polypeptide thiol ester made by the method according to claim 13 or 14 to one or more antigen proteins.
16. A method according to claim 15 comprising coupling the polypeptide to one antigen protein.
17. A method of making a concatamerised polypeptide, the method comprising expressing a concatamer according to claims 2 or 3, isolating an expressed polypeptide having a unique cysteine residue, conjugating the unique cysteine residue in the isolated polypeptide through a chemical linkage to an antigen molecule comprising one or more thiol-reactive functions.
18. A pharmaceutical composition comprising or consisting of a concatamer according to claim 4 together with a physiologically acceptable excipient or carrier.

19. A pharmaceutical composition comprising or consisting of a vector according to claim 8 which includes a concatamer according to claim 4, together with a physiologically acceptable excipient or carrier.
- 5 20. A method of inducing an immune response to an antigen in the human or animal, the method comprising administering a concatamer according to claim 4, or administering a vector according to claim 8 which includes a concatamer according to claim 4.
- 10 21. A method according to claim 20 comprising administering a pharmaceutical composition according to claim 18 or 19.

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